

### **REMARKS**

Claims 27, 30, 33, 36, 37, 43, and 47-50 are pending in the application. No claims have been amended or added. Accordingly, claims 27, 30, 33, 36, 37, 43, and 47-50 will remain pending in the application.

### ***Claim Rejections – 35 U.S.C. §103***

Claims 27, 30, 33, 36, 37, 49, and 50 are rejected under 35 U.S.C. §103(a) as allegedly obvious over U.S. Pat. No. 6,953,574 to Sobol ("Sobol") in view of EP Pat. No. 1,112,692 to Kimura ("Kimura"). Applicants respectfully disagree and traverse the rejection.

In order to make out a *prima facie* showing of obviousness, the Examiner must establish that there is some motivation in one or the other of the cited references or in the state of the art at the time the invention was made to combine the references, the combination of references must teach or suggest each and every element of the claimed invention, and there must be some reasonable expectation of success in making and using the invention.

The presently claimed invention is directed to a feed supplement comprising one or more of (i) a culture obtainable by inoculating and cultivating *Lactobacillus gasseri* OLL 2716 (FERM BP-6999) in a medium containing a whey protein derivative, wherein the whey protein derivative is selected from the group consisting of a whey protein concentrate (WPC), a whey protein isolate (WPI), a hydrolysate of the whey protein concentrate, and a hydrolysate of the whey protein isolate; (ii) *Lactobacillus gasseri* OLL 2716 (FERM BP-6999) bodies isolated from the culture (i); and (iii) a supernatant of the culture (i), wherein the supernatant is obtained by removing solid matters from the culture (i). The feed supplement of the invention is administered to livestock (e.g., calves) for its intestinal flora-improving activity, anti-diarrhea activity, antioxidant activity, weight-increasing activity, and growth-promoting effect.

The Examiner has cited Sobol, which teaches a method of producing a hydrolyzed fermented medium containing microorganisms which includes providing at least one solid plant product reduced to small pieces and mixed with sugar and biocompatible liquid such as milk for fermentation (Abstract). Applicants respectfully submit that Sobol teaches different components of the culture medium and different culture conditions from the presently claimed method. Thus, using the methods taught by Sobol does not provide a composition of the invention. Additionally, Sobol does not define the strain and species of the microorganisms, and, thus, what effect administration of their composition would have cannot be determined. Specifically, Sobol does not teach administration to calves.

The inventors of the present application have discovered a method of preparing a neutralization culturing of *L. gasseri* OLL 2716 using a medium containing a whey protein derivative. In particular, Applicants have found that, when neutralization culturing was carried out with a medium containing a whey protein derivative, the concentration of the *L. gasseri* OLL 2716 microorganisms was kept high and metabolites such as lactic acid were produced in a great amount. Accurate neutralization culturing is difficult to be carried out in a culture medium of lactic acid bacterium, milk and whey because sterilization and culture of medium cause precipitation, coagulation, and increased viscosity. In the present invention, even when sterilized culture obtained by neutralization culturing of *L. gasseri* OLL 2716 was administered to calves, intestinal flora improving effect, anti-diarrhea effect and weight increasing effects were observed. Therefore, Applicants have shown for the first time the preparation of a feed composition obtained by neutralization culturing of *L. gasseri* OLL 2716 using a medium containing a whey protein derivative.

As acknowledged at page 4 of the Office Action, "[The] Claims differ from Sobol in that the specific strain of *L. gasseri* is not disclosed, nor is the crushed form of the *L. gasseri*. The Examiner has further cited Kimura as an alleged remedy for the deficiencies of Sobol. The Office Action at page states: "It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to select for the feed supplement of Sobol et al the specific strain *L. gasseri* OLL 2716 as disclosed by EP '692 because the

specific strain is disclosed to possess pharmaceutical efficacy for food products. Applicants respectfully disagree and submit for the reasons below that there is no motivation to combine Sobol and Kimura in the manner proposed by the Examiner to achieve the presently claimed invention.

Kimura teaches the elimination of *H. pylori* in stomach by administration of living *L. gasseri* OLL 2716, which is derived from humans. However, *H. pylori* is not present in the gastrointestinal tract of calves. In support of these arguments, the Examiner's attention is invited to Jelinski et al. (Can. Vet. J. 36: 379-382, June 1995; "Jelinski," submitted in an Information Disclosure Statement filed concurrently herewith) which indicates that *H. pylori* does not exist in calves (Abstract). Jelinski found that *H. pylori* was not related to abomasal ulcer in calves, which corresponds to gastric ulcer in humans. Therefore, it is not necessary to eliminate *H. pylori* in calf gastrointestinal tract by administration of *L. gasseri*. Thus, in contrast to the Examiner's assertion, the cited references provide no motivation to administer *L. gasseri* OLL 2716 to livestock for the elimination of *H. pylori* in calf gastrointestinal tract or for any other reason.

Moreover, Applicants respectfully submit that one ordinarily skilled in the art would not be motivated to use live *L. gasseri* obtained from the intestine of a different species as a probiotic. Assuming *arguendo* one skilled in the art would select a live strain to use as a probiotic in an animal, one would select a strain obtained from the intestine of the same species of animal because there is specificity in establishment in intestine according to species of animals.

In contrast, the feed supplement of the invention has novel and unexpected effects when administered to livestock, including intestinal flora-improving activity, anti-diarrhea activity, antioxidant activity, weight-increasing activity, and growth-promoting effect. For example, Kimura does not teach or suggest improvement of flora in intestine (large intestine) of humans, let alone of calves. As indicated in International Dairy Federation (Cultured and Culture-containing Dairy Products in Health, 1999; "International Dairy Federation;" submitted in an Information Disclosure Statement filed concurrently herewith)

and Reuter (Bioscience Microflora 16(2) 43-51, 1997; submitted in an Information Disclosure Statement filed concurrently herewith), *L. gasseri* is not used as probiotics in human or animals. Even as of 2004, after the earliest priority date of the present application, the list of microorganisms indicated in International Dairy Federation as connected with beneficial probiotic and dietary products in cultured milks had remained unchanged (e.g., in Kanto, New Development of Probiotics Studies Journal of Animal Science 54(1), 58-62, 2004 which is issued by a scientific society in Japan. Thus, aside from its use for the elimination of *H. pylori* in humans, which is not applicable to livestock, *L. gasseri* OLL 2716 was not used for probiotics at the time the invention was made.

The claimed invention is based at least in part on Applicants' discovery that administering a culture of *Lactobacillus gasseri* OLL 2716 to young livestock achieves many advantageous effects, including improvement of intestinal flora, prevention of diarrhea, oxidation prevention and weight increase (e.g., in comparison to antibiotic treatment). Sobol does not teach or suggest a culture of *Lactobacillus gasseri* OLL 2716 and/or the products from such a culture nor is there any motivation to combine Sobol and Kimura.

Thus, there is nothing in either of the cited references or in the state of the art at the time the invention was made that provides one of ordinary skill in the art with motivation to combine the references in the manner proffered by the Examiner. The combination of the cited references does not put one of ordinary skill in the art in possession of the claimed invention, and, therefore, one of ordinary skill in the art would not have a reasonable expectation of success in making and using the claimed invention.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 27, 30, 33, 36, 37, 49, and 50 under 35 U.S.C. §103(a).

Claims 43, 47, 48, and 50 are rejected under 35 U.S.C. §103(a) as allegedly obvious over U.S. Pat. Appl. Publ. No. 20020146399 to Raczek ("Raczek") in view of Sobol and Kimura. Applicants respectfully disagree and traverse the rejection.

The Office Action at page 6 states: "It would have been obvious to one of ordinary skill in the art to select for the method of Raczek the feed supplement of Sobol et al using the specific strain of EP '692 to improve intestinal flora of a young livestock such as a calf because the prior art clearly teach that *L. gasseri* is useful in animal feed and the strain OLL 2716 has also shown success in food as well." Applicants respectfully disagree.

The Examiner has alleged that it would be obvious to substitute the composition of Sobol in the method of Raczek. However, as set forth above, there is nothing in the cited references that provides one of ordinary skill in the art with motivation to combine Sobol and Kimura in the manner proposed by the Examiner. Nor does Raczek remedy the deficiencies of Sobol and Kimura or provide a motivation to combine the cited references.

Therefore, because the cited combination of references does not put one of ordinary skill in the art in possession of the claimed invention, one of ordinary skill in the art would not have a reasonable expectation of success in making and using the claimed invention.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 43, 47, 48, and 50 under 35 U.S.C. §103(a).

### **CONCLUSION**

In view of the foregoing amendments and arguments, Applicants respectfully request reconsideration and withdrawal of all pending objections/rejections and allowance of the application with claims 27, 30, 33, 36, 37, 43, and 47-50 presented herein. If a telephone call with Applicants' representative would be helpful in expediting prosecution of the application, Applicants invite the Examiner to contact the undersigned at the telephone number shown below.

The Director is hereby authorized to charge any credits or deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to Deposit Account No. 04-1105, under Order No. 64291(71719).

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Respectfully submitted,

Electronic signature: /Elbert Chiang, Ph.D./  
Elbert Chiang, Ph.D.

Registration No.: 60,325

EDWARDS ANGELL PALMER & DODGE  
LLP

P.O. Box 55874

Boston, Massachusetts 02205

(617) 239-0100

Attorneys/Agents For Applicant